Meeting Summary:
Scientific Advances in Trichotillomania and Related Body-Focused Repetitive Behaviors

National Institute of Mental Health
Co-sponsored
by Trichotillomania Learning Center, Inc.

A roundtable discussion held November 4–5, 2004, reviewed research on trichotillomania and related body-focused repetitive behavior. Twenty-two trichotillomania experts from various scientific disciplines — including psychology, psychiatry, dermatology, neurobiology, and animal sciences — discussed promising approaches and opportunities for clinical research in trichotillomania. They highlighted potentially promising avenues that require further development.

The first talk was an overview of etiological theories of trichotillomania, including psychoanalytic, cognitive-behavioral, and biological theories. Cognitive-affective neuroscience was introduced as a context, providing a translational approach to brain-mind processes involved in trichotillomania (e.g., fear conditioning). The focus was on "simple" cognitive-affective processes and neurocircuitry, and possible models or approaches to trichotillomania were described, such as: motor program control/chunking of action; response to stress/regulation of affect; and response inhibition/salience attribution.

In models of program control, there is potential involvement of the basal ganglia and striatum, such that lesions in the fronto-striatal circuits may disrupt implicit learning and lead to involuntary motor symptoms as well as obsessions and compulsions. Several potentially related endophenotypes were described, including neonatal hypoxia, hoxB8 variant, and D8/17 antigen. Increased dopamine firing was implicated as a neurochemical abnormality relating to this approach.

The stress response/affect regulation model was also described, which involves fear conditioning that is mediated by amygdala-hippocampal circuitry. In this model, skin is a neuro-immuno-cutaneous-endocrine (NICE) bi-directional interface. An example was given in which the combination of cognitive impairment and environmental deprivation leads to stereotyped behavior in developmental disorders. Genetic and epigenetic factors were discussed, such as the potential involvement of the serotonin transporter gene (5-HTTP) in relation to fear processes and catechol-O-methyltransferase (COMT) in relation to pain regulation. Regarding neurochemistry, there is possible involvement of dopamine, opioids, analgesics, and cortisol.

An approach involving reduced impulse control and increased reward seeking was explored, wherein repeated behavior is overlearned and indicative of positive reinforcement. Preclinically, the orbitofrontal cortex and nucleus accumbens were implicated, due to their role in impulsivity and reward-seeking behavior. Endophenotypes involving substance abuse and both dopamine and opioid variants were hypothesized.

Pathological processes that best characterize trichotillomania were discussed, including characterizing trichotillomania as “chunks” of grooming, as a stress response/affect regulation disorder, or as an impulsive control disorder/addition. These approaches overlap developmentally, neurologically, and neuropsychologically. Limitations of these approaches include the need to answer questions regarding the development of trichotillomania, gender differences, the neurobiology of treatments such as habit reversal and extinction, heterogeneity of the disorder, evolutionary factors, and other genetic influences on the disorder. Current research in neuronal and molecular bases of stereotypic behavior may be useful.

The second talk focused on animal models of trichotillomania. Different animal models have different strengths and weaknesses. Induced models can be powerful tools for investigating single etiologies and particular physiological pathways — but these strengths can limit their applicability to disorders with complex etiologies. Spontaneous models, while widespread in somatic medicine, are rare in psychiatric research — not least because they are far harder to validate. However spontaneous models are particularly well suited to dissecting complex etiologies. Fur and feather pulling are common abnormal behaviors in many animal species, and although several examples have been suggested as possible spontaneous models of trichotillomania, none have been formally validated.

Certain strains of laboratory mice are prone to a behavior called “barbering” — where one or more mice in the cage begin to pluck idiosyncratic repeated patterns of fur or whiskers from their cagemates. Barbering shows interesting phenomenological, epidemiological, and neuropsychological similarities to trichotillomania. Thus barbering behavior is focused, goal-directed, and often accompanied by oral manipulation of the plucked fur. Singly housed mice self-pluck, and established barbers self-pluck when removed from their victims. Barbering is more common in females, first appears around puberty, and is more common in reproductively active mice. Barbering mice show a specific neuropsychological deficit whereby, like many obsessive-compulsive spectrum disorders (including trichotillomania), the severity of barbering “symptoms” is correlated with the severity of stuck-in-set perseveration measured in a standard set-shifting task. In parallel, other researchers have reported that Hoxb8 knockout mice perform an intense form of this behavior and have similarly suggested that these mice might be an induced model of trichotillomania.

Key issues identified during discussion were: 1) do the spontaneous barbering model and the induced Hoxb8 model ultimately involve similar functional mechanisms? and 2) are there trichotillomania subtypes (e.g., stereotyped plucking) that are not well modeled by these mice and might be better addressed with other models (e.g., acral lick dermatitis)? The roundtable concluded that these mice models promise to help identify genetic and environmental etiologies, basic physiological mechanisms, and future therapies.

A third talk focused on therapeutic interventions. Discussion included the definition of outcomes, extant treatment literature, and issues relevant to future directions for treatment research on trichotillomania. The ultimate outcome goals are: 1) to find a cure for the disorder, such that symptoms are eliminated and durable remission maintained even after discontinuation of therapy; and 2) primary prevention. Current treatment goals are: 1) control of symptoms (core symptoms such as hair-pulling and urge) as well as comorbidities, and 2) prevention of relapse.

The literature of pharmacological treatments included studies with selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), neuroleptics, and other medications, such as lithium and naltrexone. Psychotherapeutic treatment approaches were also discussed, including psychoeducation, mindfulness, and cognitive therapy (e.g., thought stopping, restructuring defusion from literal language, and guided self-dialogue). Behavioral treatments were also outlined, including habit reversal, self-monitoring, stimulus control, competing behavior, relaxation, and reinforcement.

Trichotillomania may be classified as an impulse control disorder, obsessive-compulsive spectrum disorder, or habit/stereotypy. Hair-pulling may exist as either a habit or goal-directed behavior. Habits are repetitive behaviors or routine actions occurring without conscious effort. They are driven by learning of associations, and suggestive evidence points to the involvement of the dorsolateral striatum. Goal-directed behavior is more dependent on response-outcome than stimulus-response and may involve the frontal lobe, the dorsomedial striatum, and accumbens.

The roundtable discussed future directions for research, including improvements in defining and measuring trichotillomania, exploring etiopathophysiology, better knowledge of the treatment of acute episodes, and development of evidence-based sequential treatment algorithms.

Breakout sessions focused on neurobiology (including genetics, imaging, and animal models) and interventions and therapeutics (pharmacotherapy, behavior therapy).

Trichotillomania Neurobiology Research

The workgroup on neurobiology discussed the need to further describe the behavioral phenomenology of trichotillomania in order to better specify neurobiological areas for research. The group described the need for better delineation of the onset of the behavior versus the reinforcement of the behavior. The workgroup agreed that animal models are sought — with a caveat due to the type of behaviors involved in trichotillomania. Concerns revolved around the approach used to describe individual symptoms (such as the sensory urge involvement) and whether to describe them as repetitive behavior, stereotypic behavior, goal-directed behavior, self-injurious behavior, and/or reward seeking behavior.

Differentiation of stereotypic versus goal-directed aspects of behavior was also emphasized, and use of rodent work was judged an excellent way to parse out initiation from maintenance of behavior. Further research on the behavior of barbering mice (versus outcome of fur/whisker loss) was recommended in order to answer questions about the possibility of inducing or manipulating the behavior. The group discussed the possibility of framing trichotillomania as a disorder of addiction, which incorporates the sensory urge abnormality and craving. There was a suggestion to consider possible contributions from the literature on phantom limb phenomena.

Specific Recommendations about Neurobiology Research

Areas for future research to locate specific brain circuitry involved included:

- Symptom provocation studies with fMRI
- Imaging studies with discordant twin samples
- Pharmacologic challenge studies

- Endocrinology studies (e.g., investigating changes at pubarche) that include genetic studies, studies of knock-out mice, of hormonal manipulation in mice, and of breeding versus non-breeding mice
- Studies of the phenomenology of trichotillomania — as a prerequisite for all neurobiological research — to better define phenotypes and endophenotypes of the disorder.
- Research on gene-environment interactions, highlighted the difficulty of parsing out the causal versus correlational relationships

---

Trichotillomania Interventions Research

The interventions working group also emphasized the need to clarify diagnostic criteria for the disorder. Of particular concern was the frequent failure to record the required diagnostic criteria of tension prior to pulling out hair or during attempts to resist the behavior. This led to a focus on the need for better definitions of the apparent subtypes of trichotillomania, for better diagnostic criteria, for better understanding of the course of the disorder over development, and for better predictors of outcome. In addition, the development of comprehensive assessment scales was recommended.

The working group suggested epidemiologic studies to determine the prevalence of the disorder as well as environmental variables that may increase risk. The group also recommended a broad multidisciplinary paper on trichotillomania that could summarize research to date on clinical phenomenology, etiology, and neurobiological research.

Specific recommendations about treatment research

- Research on functional variables related to trichotillomania (e.g., habit, emotion regulation)
- A consortium for the systematic evaluation of pharmacological interventions that could incorporate interventions under study into clinical protocols
- Larger randomized clinical trials to evaluate enhancements to current behavior therapy relative to treatment as usual, as well as studies of the combination of behavior therapy and pharmacologic agents
- Animal research for developing novel pharmacological approaches, along with studies of mechanisms of change
- Coordination with private organizations such as the Trichotillomania Learning Center to help establish consensus on phenomenology, assessment development, and diagnostic criteria

---

General Next Steps for Trichotillomania Research

1) Refinement of definitions of the phenomenology, including the number of subtypes and their descriptions.
2) Studies of common comorbidities and associated conditions.
3) Epidemiologic studies to determine prevalence, incidence, and patterns of presentation as well as associated impact and impairment.

4) Studies of etiology, including gene-environment interaction research in both animals and humans, as well as neuroimaging studies (i.e., fMRI).

5) Parallel to the other steps, treatment research that includes developing treatment guidelines and manualizing treatments, and research on treatment resistance. This may also include research on service delivery in community and school settings.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH • NATIONAL INSTITUTE OF MENTAL HEALTH

NIMH
National Institute of Mental Health

April 2005